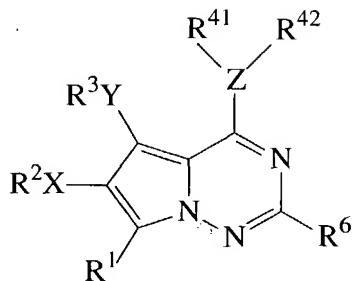


What is Claimed is:

1. A compound of formula (I)



5

(I)

wherein

Z is selected from the group consisting of O, S, N, OH, and Cl, with the provisos that when Z is O or S, R⁴¹ is absent, and when Z is OH or Cl, both R⁴¹ and R⁴² are absent, and when Z is N, then R⁴¹ is H;

X and Y are independently selected from the group consisting of O, OCO, S, SO, SO₂, CO, CO₂, NR¹⁰, NR¹¹CO, NR¹²CONR¹³, NR¹⁴CO₂, NR¹⁵SO₂, NR¹⁶SO₂NR¹⁷, SO₂NR¹⁸, CONR¹⁹, halogen, nitro and cyano, or X or Y are absent;

R¹ is hydrogen, CH₃, OH, OCH₃, SH, SCH₃, OCOR²¹, SOR²², SO₂R²³, SO₂NR²⁴R²⁵, CO₂R²⁶, CONR²⁷R²⁸, NH₂, NR²⁹SO₂NR³⁰R³¹, NR³²SO₂R³³, NR³⁴COR³⁵, NR³⁶CO₂R³⁷, NR³⁸CONR³⁹R⁴⁰, halogen, nitro, or cyano;

R² and R³ are independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, aralkyl, substituted aralkyl, heteroaryl, substituted heteroaryl, heterocycloalkyl or substituted heterocycloalkyl; with the proviso that when X is halo, nitro or cyano, R² is absent, and, when Y is halo, nitro or cyano, R³ is absent;

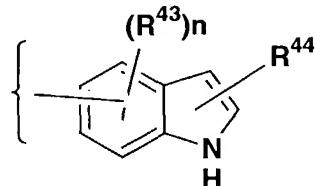
R⁶ is H, alkyl, substituted alkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, NR⁷R⁸, OR⁹ or halogen;

R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²¹, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, R³⁰, R³¹, R³², R³⁴, R³⁵, R³⁶, R³⁸, R³⁹ and R⁴⁰ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl,

heteroaryl, substituted heteroaryl, heterocyclo, or substituted heterocyclo;

R²², R²³, R³³ and R³⁷ are independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclo, or substituted heterocyclo;

5 R⁴² is



(R⁴³)_n wherein n equals 0, 1 or 2 and each R⁴³ is independently selected from the group consisting of hydrogen, fluorine, chlorine and methyl; and

10 R⁴⁴ is methyl, or hydrogen,

with the further provisos that:

- a. R² may not be hydrogen if X is SO, SO₂, NR¹³CO₂, or NR¹⁴SO₂; and
- b. R³ may not be hydrogen if Y is SO, SO₂, NR¹³CO₂, or NR¹⁴SO₂;

or an enantiomer, diastereomer, or pharmaceutically acceptable salt, prodrug, or

15 solvate thereof,

2. A compound according to claim 1 wherein R¹ is hydrogen or methyl; R⁶ is hydrogen; R³ is lower alkyl; and Z is oxygen or nitrogen.

20 3. A compound according to claim 1 wherein R¹ is hydrogen; R³ is lower alkyl; Y is absent; X is oxygen or nitrogen; R⁴³ is fluoro or hydrogen; and R⁴⁴ is hydrogen or methyl.

25 4. A compound according to claim 1 wherein X is oxygen; R² is a substituted alkyl and R⁴³ is fluoro.

5. A compound selected from the group consisting of
4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-ol,

1-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methy-pyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-4-(aminosulfonyl)aminobutan-2-ol,

N-{3-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methy-pyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-2-Hydroxy-propyl}-methanesulfonamide,

5 (2*S*)-3-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methy-pyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-propane-1,2-diol,

(2*R*)-3-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-propane-1,2-diol,

(2*R*)-1-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-propan-2-ol,

10 (2*S*)-1-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-propan-2-ol,

(2*R*)-1-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-3-methoxy-propan-2-ol,

15 (2*S*)-1-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-3-methoxy-propan-2-ol,

2-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-ethanol,

N-{2-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-ethyl}-methanesulfonamide,

20 (2*R*)-1-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methy-pyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-4-methanesulfonyl-butan-2-ol,

(2*S*)-1-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methy-pyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-4-methanesulfonyl-butan-2-ol,

25 5-Methyl-4-(2-methyl-*1H*-indol-5-yloxy)-6-(3-piperidin-1-ylpropoxy)-pyrrolo[2,1-f][1,2,4]triazine,

4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methyl-6-(2-piperidin-4-yl-ethoxy)-pyrrolo[2,1-f][1,2,4]triazine,

30 4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methyl-6-(3-pyridin-4-yl-propoxy)-pyrrolo[2,1-f][1,2,4]triazine,

{1-[4-(4-Fluoro-2-methyl-*1H*-indol-5-yloxy)-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yloxymethyl]-3-methanesulfonyl-propyl}-dimethyl-amine, 71

2-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-1-methylethylamine,
 {2-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-1-methylethyl}-methylamine,
 5 4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methyl-6-(morpholin-2-ylmethoxy)-pyrrolo[2,1-f][1,2,4]triazine,
 [(1*R*),2*S*]-2-Dimethylaminopropionic acid-[2-[4-(4-fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]]-1-methylethyl ester,
 [(1*R*), 2*S*]-2-Amino-4-methylpentanoic acid [2-[4-(4-fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]]-1-methylethyl ester,
 10 [(1*R*), 2*S*]-2-Aminopropionic acid 2-[4-(4-fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-1-methylethyl ester,
 4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-6-(3-methanesulfonyl-propoxy)-5-methyl-pyrrolo[2,1-f][1,2,4]triazine, and
 15 N-{3-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-propyl}-methanesulfonamide.

6. A compound selected from the group consisting of
 4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-
 20 6-ol,
 (2*S*)-3-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-propane-1,2-diol,
 (2*R*)-3-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-propane-1,2-diol,
 25 (2*R*)-1-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-propan-2-ol,
 (2*S*)-1-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-propan-2-ol,
 (2*R*)-1-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-3-methoxy-propan-2-ol,
 30 (2*S*)-1-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-3-methoxy-propan-2-ol,

5-Methyl-4-(2-methyl-1*H*-indol-5-yloxy)-6-(3-piperidin-1-ylpropoxy)-pyrrolo[2,1-f][1,2,4]triazine,

4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methyl-6-(2-piperidin-4-yl-ethoxy)-pyrrolo[2,1-f][1,2,4]triazine,

5 2-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-1-methylethylamine,

[(1*R*),2*S*]-2-Dimethylaminopropionic acid-[2-[4-(4-fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f]-[1,2,4]triazin-6-yloxy]]-1-methylethyl ester,

[(1*R*), 2*S*]-2-Amino-4-methylpentanoic acid [2-[4-(4-fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]]-1-methylethyl ester,

10 [(1*R*), 2*S*]-2-Aminopropionic acid 2-[4-(4-fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-1-methylethyl ester,

4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-6-(3-methanesulfonyl-propoxy)-5-methyl-pyrrolo[2,1-f][1,2,4]triazine, and

15 N-{3-[4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methyl-pyrrolo[2,1-f][1,2,4]triazin-6-yloxy]-propyl}-methanesulfonamide.

7. A pharmaceutical composition comprising at least one of the compounds of Claim 1 and a pharmaceutically acceptable carrier therefor.

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8. A pharmaceutical composition comprising at least one of the compounds of Claim 5 and a pharmaceutically acceptable carrier therefor.

25

9. A pharmaceutical composition comprising at least one of the compounds of Claim 6 and a pharmaceutically acceptable carrier therefor.

10. A pharmaceutical composition comprising at least one or more compounds of Claim 1 in combination with a pharmaceutically acceptable carrier and at least one additional anti-cancer or cytotoxic agent.

30

11. A pharmaceutical composition comprising at least one or more compounds of Claim 5 in combination with a pharmaceutically acceptable carrier and

at least one additional anti-cancer or cytotoxic agent.

12. A pharmaceutical composition comprising at least one or more compounds of Claim 6 in combination with a pharmaceutically acceptable carrier and
5 at least one additional anti-cancer or cytotoxic agent.

13. The pharmaceutical composition of Claim 8, wherein said anti-cancer or cytotoxic agent is selected from the group consisting of: linomide, inhibitors of integrin $\alpha v\beta 3$ function, angiostatin, razoxane, tamoxifen, toremifene, raloxifene,
10 droloxifene, iodoxifene, megestrol acetate, anastrozole, letrozole, borazole, exemestane, flutamide, nilutamide, bicalutamide, cyproterone acetate, gosereline acetate, leuprolide, finasteride, herceptin, metalloproteinase inhibitors, inhibitors of urokinase plasminogen activator receptor function, growth factor antibodies, growth factor receptor antibodies, bevacizumab, cetuximab, tyrosine kinase inhibitors,
15 serine/threonine kinase inhibitors, methotrexate, 5-fluorouracil, purine, adenosine analogues, cytosine arabinoside, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-C, dactinomycin, mithramycin, cisplatin, carboplatin, nitrogen mustard, melphalan, chlorambucil, busulphan, cyclophosphamide, ifosfamide, nitrosoureas, thiotapec, vincristine, paclitaxel, docetaxel, epothilone analogs, discodermolide
20 analogs, eleutherobin analogs, etoposide, teniposide, amsacrine, topotecan, irinotecan, flavopyridols, proteasome inhibitors including bortezomib and biological response modifiers.

14. A method for producing an antiangiogenic effect which comprises
25 administering to a mammalian species in need thereof, an effective antiangiogenic producing amount of at least one of the compounds of Claim 1.

15. A method for producing a vascular permeability reducing effect which comprises administering to a mammalian species in need thereof an effective vascular
30 permeability reducing amount of at least one of the compounds of Claim 1.

16. A method of inhibiting protein kinase activity of growth factor

receptors which comprises administering to a mammalian species in need thereof, an effective protein kinase inhibiting amount of at least one of the compounds of Claim 1.

5 17. A method of inhibiting tyrosine kinase activity of growth factor receptors which comprises administering to a mammalian species in need thereof, an effective tyrosine kinase inhibiting amount of at least one of the compounds of Claim 1.

10 18. A method for treating proliferative diseases, comprising administering to a mammalian species in need thereof, a therapeutically effective amount of the composition of Claim 7.

15 19. A method for treating cancer, comprising administering to a mammalian species in need thereof, a therapeutically effective amount of the composition of Claim 7.

20 20. A method for treating inflammation, comprising administering to a mammalian species in need thereof, a therapeutically effective amount of the composition of Claim 7.

25 21. A method for treating autoimmune diseases, comprising administering to a mammalian species in need thereof, a therapeutically effective amount of the composition of Claim 7.

22. A method for treating proliferative diseases, comprising administering to mammalian species in need thereof, a therapeutically effective amount of the composition of Claim 7.

30 23. A method for treating cancer, comprising administering to a mammalian species in need thereof, a therapeutically effective amount of the composition of Claim 7.

24. A method for treating inflammation, comprising administering to a mammalian species in need thereof, a therapeutically effective amount of the composition of Claim 7.

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25. A method for treating autoimmune diseases, comprising administering to a mammalian species in need thereof, a therapeutically effective amount of the composition of Claim 7.

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26. A method for treating diseases associated with signal transduction pathways operating through growth factor receptors, which comprises administering to a mammalian species in need thereof a therapeutically effective amount of at least one of the compounds of Claim 1.